REMARKS

Reconsideration is respectfully requested in light of the following remarks.

Claims 1-11, 14, and 16-19 are before the Examiner. Claims 7-9, 11 and 18-19 remain withdrawn from consideration.

not attached Please find enclosed a recent response filed with the EPO where issues similar to those present here are addressed. See Attachment A. The art relied upon by the European Examiner was previously submitted to the USPTO in an IDS filed August 31, 2000 and was indicated to have been considered. See paper No. 14.

Rejections under 35 USC 103

Claims 1-6, 10 and 12-17 are rejected under 35 USC 103 as being unpatentable over Ko (5,851,528) by itself or in combination with De Lacharrier (5,744,156). Claims 1-6, 10 and 12-17 are rejected under 35 USC 103 as being unpatentable over Ko (5,851,528) by itself or in combination with De Lacharrier (5,744,156), in further combination with applicants' statements of prior art. Applicant respectfully traverses both rejections.

It is respectfully submitted that the statements of rejection fail to establish a prima facie case of obviousness.

Claim 1 is directed to a method for treating the symptoms of an immediate hypersensitivity reaction caused by polyethoxylated oil- or a derivatized polyethoxylated oil-carrier. The method includes the step of administering to a subject a hypersensitivity reducing

effective amount of a complement activation inhibitor along with the composition containing the carrier and the active ingredient.

Ko teaches chimeric molecules composed of a first and second polypeptides, both of which inhibit complement activation. The chimeric proteins are taught to reduce inflammation. Conditions mentioned include those associated with ischemia-reperfusion, crash injury, burns, ARDS, autoimmune disorders, etc.. Table 1, referred to by the Examiner, lists potential clinical targets of the protein chimeras, i.e. targets to try. [1] None is an immediate complement reaction like that claimed. While the Table does mention "Drug Allergy", drug allergies come in a variety of types, e.g. delayed and causes. Note background section of the specification. This teaching does not equate with a teaching of "an immediate hypersensitivity reaction caused by polyethoxylated oil- or a derivatized polyethoxylated oil-carrier", a non-drug.

Accordingly, the teaching of Klaasen (Table1) merely suggest potential applications, e.g. "Allergic Reactions" to drugs, which have characteristics and a causality that are distinctly different from the claimed "immediate complement reactions".

De Lacharriere teaches the use of a substance P antagonist for the preparation of a pharmaceutical composition for treating skin reddening of a neurological origin. There is no

[1] The art of pathological conditions associated with complement activation in the field of complement prior to the instant disclosed invention are described in previously submitted Table A. Applicants consulted 44 reviews, research, or textbook articles in the field. Many of these reviews, both before and after 1998 (the Ko, et al patent issued on 22 Dec 98), gave comprehensive listing of pathological conditions associated with complement activation. Each of the pathological conditions mentioned by Ko, et al are included. The first mention of immediate non-IgE hypersensitivity reactions mediated by complement was published by Applicants in Feb, 1998.

mention of an immediate hypersensitivity reaction associated with complement activation by amphiphilic molecules nor its treatment in the manner claimed.

There is no teaching suggestive of the invention as claimed.

It is noted that the Examiner makes reference to an admission. It is assumed that the Examiner is referencing Applicants' characterization of the prior art. This is not the type of admission referred to in MPEP ¶¶ 706.02(c), 2129 and 2133.03(c) and the case law cited therein. Further, the characterization of the prior art is demonstrating the "uncertainty" as to causality relative to terms of Cremopor and taxol.

There is no admission by Applicants that Cremophor EL causes complement activation present in the specification as filed. There is no disclosure of a teaching that conclusively link the presence of Cremophor to complement activation. A fair reading of the instant specification's background section including pages 5 and 6 suggests the immune pathomechanism of hypersensitivity to taxol and the individual roles that pacitaxel and Cremophor EL play in the reaction remain obscure. It is clear from the specification that there remains some 0.9% of patients develop a severe, life threatening reaction that precludes further treatment with liposome entrapped drugs. It is also clear that Applicants were of the opinion that the reported literature suggested the need for additional work, which Applicants did, needed to be done regarding the establishment of a causal role of complement, liposome activation and cardiopulmonary reaction. This is not an admission against interest. This "admission" does not supplement the deficiencies of the Ko and De Lacharriere references.

Further, it is submitted that the state of the art as described by Applicants in the background section suggests that at the time the application was filed there would not have been a reasonable expectation of success for reducing the symptoms of polyethoxylated oil induced hypersensitivity, an immediate hypersensitivity reaction, through the inclusion of an complement activation inhibitor along with a Cremophor EL and taxol.

The teachings of references, taken alone or in combination, are incomplete and thereby fail to suggest the claimed invention.

Further, it is respectfully submitted that the references fail to suggest their combination. There is no problem evident in one for which the other is a solution.

In addition, please note that the European Examiner references D5 (Terwogt et al previously submitted, supra) as showing the recognition of Cremophor as causing adverse effects and suggests its removal from the formula as the solution to this problem. This is not the approach taken by Applicants nor is it suggestive of the claimed method.

Since a prima facie case has not been established, withdrawal of the rejection is respectfully requested.

Conclusion

Having addressed all of the rejections and objections, allowance of the application is believed to be in order. A notice to this effect is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 210-380 referencing docket no. 38644-170639 (formerly 378332000900). However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

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